

Claims

1. A microdevice, which microdevice comprises:

- a) a substrate; and
- b) a photorecognizable coding pattern on said substrate,

wherein said microdevice does not comprise an anodized metal surface layer.

2. The microdevice of claim 1, wherein the substrate comprises a material that is selected from the group consisting of a silicon, a plastic, a glass, a ceramic, a rubber, a polymer and a combination thereof.

3. The microdevice of claim 2, wherein the silicon is silicon dioxide or silicon nitride.

4. The microdevice of claim 1, wherein the substrate comprises a surface that is hydrophobic or hydrophilic.

5. The microdevice of claim 1, wherein the shape of the substrate is selected from the group consisting of sphere, square, rectangle, triangle, circular disc, cube-like shape, cube, rectangular parallelepiped (cuboid), cone, cylinder, prism, pyramid, right-angled circular cylinder and other regular or irregular shape.

6. The microdevice of claim 1, wherein the thickness of the substrate is from about 0.1 micron to about 10 microns.

7. The microdevice of claim 5, wherein the substrate is a rectangle having a surface area from about 10 squared-microns to about 10,000 squared-microns.

8. The microdevice of claim 5, wherein the substrate is a circular disc having a diameter from about 3 microns to about 500 microns.

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9. The microdevice of claim 5, wherein the substrate is in a cube-like shape having a side width from about 10 microns to about 100 microns.

5 10. The microdevice of claim 5, wherein the substrate is in an irregular shape having a single-dimension from about 1 micron to about 500 microns.

11. The microdevice of claim 1, wherein the substrate comprises a silicon layer and a metal layer.

10 12. The microdevice of claim 11, wherein the metal layer is an aluminum layer.

13. The microdevice of claim 11, wherein the metal layer comprise a magnetic material.

15 14. The microdevice of claim 11, wherein the metal layer comprise nickel metal or CoTaZr (Cobalt-Tantalum-Zirconium) alloy.

20 15. The microdevice of claim 1, wherein the photorecognizable coding pattern is the material composition of the substrate itself, a hole in the substrate or a substance immobilized on the substrate, said substance having an optical refractive property that is different from the optical refractive property of the substrate.

25 16. The microdevice of claim 15, wherein the versatility of the photorecognizable coding pattern is caused by the shape, number, position distribution, optical refractive property, material composition, or a combination thereof, of the substrate, the hole(s), or the substance(s) immobilized on the substrate.

30 17. The microdevice of claim 15, wherein the photorecognizable coding pattern comprises a plurality of the holes and/or a plurality of the substances.

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18. The microdevice of claim 1, wherein the photorecognizable coding pattern is fabricated or microfabricated on the substrate.

5 19. The microdevice of claim 1, wherein the photorecognizable coding pattern is lithographically patterned.

10 20. The microdevice of claim 19, wherein the lithographical pattern is selected from the group consisting of photolithography, electron beam lithography and X-ray lithography.

21. The microdevice of claim 15, wherein the substance is deposited on the substrate.

15 22. The microdevice of claim 15, wherein the substance is comprised within the substrate.

23. The microdevice of claim 15, wherein the substance is deposited by evaporation or sputtering.

20 24. The microdevice of claim 1, further comprising a binding partner that is capable of binding to a moiety to be manipulated.

25 25. The microdevice of claim 24, wherein the binding partner specifically binds to the moiety.

A2 26. The microdevice of claim 24, wherein the binding partner is selected from the group consisting of a cell, a cellular organelle, a virus, a molecule and an aggregate or complex thereof.

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27. The microdevice of claim 24, which comprises a plurality of binding partners, each binding partner is capable of binding or specifically binding to a different moiety to be manipulated.

5 28. The microdevice of claim 1, further comprising an element that facilitates and/or enables manipulation of the microdevice and/or a moiety/microdevice complex.

10 29. The microdevice of claim 28, wherein the element is selected from the group consisting of a magnetic material, a conductive or insulating material, a material having high or low acoustic impedance and a charged material.

15 30. The microdevice of claim 28, wherein the element facilitates and/or enables manipulation of the microdevice and/or a moiety/microdevice complex by a physical force selected from the group consisting of a dielectrophoresis, a traveling-wave dielectrophoresis, a magnetic, an acoustic, an electrostatic, a mechanical, an optical radiation and a thermal convection force.

20 31. The microdevice of claim 28, which comprises a plurality of the elements, each of the elements facilitates and/or enables manipulation of the microdevice and/or the moiety/microdevice complex by a different physical force.

25 32. The microdevice of claim 24, further comprising an element that facilitates and/or enables manipulation of the microdevice and/or the moiety/microdevice complex.

30 33. The microdevice of claim 1, further comprising a detectable marker or a molecular tag.

34. The microdevice of claim 33, wherein the detectable marker is a dye, a radioactive substance or a fluorescent substance.

35. A method for isolating a moiety, which method comprises:
a) providing a microdevice comprising a substrate, a photorecognizable coding pattern on said substrate and a binding partner that is capable of binding to a moiety to be isolated, wherein said microdevice does not comprise an anodized metal surface layer;

b) contacting a sample containing or suspected of containing of said moiety with said microdevice provided in step a) under conditions allowing binding between said moiety and said binding partner; and

c) recovering said microdevice from said sample,
whereby the identity of said isolated moiety is assessed by photoanalysis of said photorecognizable coding pattern.

36. The method of claim 35, wherein the moiety is a cell, a cellular organelle, a virus, a molecule and an aggregate or complex thereof.

37. The method of claim 35, wherein a plurality of moieties are isolated by using a plurality of microdevices, each of the microdevices contains a binding partner that is capable of binding to a member of the plurality of the moieties.

38. The method of claim 35, wherein the sample is a fluid sample.

39. The method of claim 35, wherein the isolation is conducted in a liquid container selected from the group consisting of a beaker, a flask, a cylinder, a test tube, an enpindorf tube, a centrifugation tube, a culture dish, a multiwell plate and a filter device, or conducted in a chip format.

40. The method of claim 35, further comprising a step of recovering said isolated moiety from said microdevice.

41. The method of claim 35, wherein the binding partner specifically binds to the moiety.

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42. A method for manipulating a moiety, which method comprises:

a) providing a microdevice comprising a substrate, a photorecognizable coding pattern on said substrate and a binding partner that is capable of binding to a moiety to be manipulated, wherein said microdevice does not comprise an anodized metal surface layer;

b) coupling said moiety to said microdevice provided in step a) via binding between said moiety and said binding partner to form a moiety-microdevice complex; and

c) manipulating said moiety-microdevice complex with a physical force in a chip format or in a non-chip format, thereby said moiety is manipulated.

43. The method of claim 42, wherein the manipulation is effected through a combination of a structure that is external to the chip and a structure that is built-in in the chip.

44. The method of claim 42, wherein the moiety to be manipulated is selected from the group consisting of a cell, a cellular organelle, a virus, a molecule and an aggregate or complex thereof.

45. The method of claim 42, wherein the physical force is selected from the group consisting of a dielectrophoresis, a traveling-wave dielectrophoresis, a magnetic, an acoustic, an electrostatic, a mechanical, an optical radiation and a thermal convection force.

46. The method of claim 42, wherein the manipulation is selected from the group consisting of transportation, focusing, enrichment, concentration, aggregation, trapping, repulsion, levitation, separation, fractionation, isolation and linear or other directed motion of the moiety.

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47. The method of claim 42, wherein the moiety is not directly manipulatable by a physical force.

5 48. The method of claim 42, wherein neither the moiety nor the binding partner is directly manipulatable by a physical force, and the microdevice contains an element that makes the microdevice or the moiety-microdevice complex manipulatable.

49. The method of claim 42, wherein a plurality of moieties is manipulated.

10 50. The method of claim 49, wherein the plurality of moieties is manipulated via a plurality of corresponding microdevices.

15 51. The method of claim 49, wherein the plurality of moieties is manipulated sequentially or simultaneously.

52. The method of claim 42, further comprising a step of recovering said manipulated moiety from said microdevice and/or said chip.

20 53. The method of claim 42, further comprising a step of assessing the identity of the manipulated moiety by photoanalysis of the photorecognizable coding pattern of the microdevice.

25 54. The method of claim 52, further comprising a step of assessing the identity of the recovered moiety by photoanalysis of the photorecognizable coding pattern of the microdevice.

55. The method of claim 42, wherein the binding partner specifically binds to the moiety.

30 56. A kit for manipulating a moiety, which kit comprises:

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a) a microdevice comprising a substrate, a photorecognizable coding pattern on said substrate and a binding partner that is capable of binding to a moiety to be manipulated, wherein said microdevice does not comprise an anodized metal surface layer; and

5 b) a chip on which a moiety-microdevice complex can be manipulated.

10 57. The kit of claim 56, further comprising instruction(s) for coupling the moiety to the microdevice and/or for manipulating the moiety-microdevice complex on the chip.

15 58. A method for detecting a moiety, which method comprises:

a) providing a microdevice comprising a substrate, a photorecognizable coding pattern on said substrate and a binding partner that is capable of binding to a moiety to be detected, wherein said microdevice does not comprise an anodized metal surface layer;

b) contacting a sample containing or suspected of containing of said moiety with said microdevice provided in step a) under conditions allowing binding between said moiety and said binding partner; and

20 c) detecting binding between said moiety and said binding partner, in a chip format or in a non-chip format, whereby the presence or amount of said moiety is assessed by analysis of binding between said moiety and said binding partner and the identity of said moiety is assessed by photoanalysis of said photorecognizable coding pattern.

25 59. The method of claim 58, wherein the moiety is a cell, a cellular organelle, a virus, a molecule and an aggregate or complex thereof.

30 60. The method of claim 58, wherein a plurality of moieties is detected by using a plurality of microdevices, each of the microdevices contains a binding partner that is capable of binding to a member of the plurality of the moieties.

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61. The method of claim 58, wherein the sample is a fluid sample.

5 62. The method of claim 58, wherein the sample is contacted with the microdevice in a liquid container selected from the group consisting of a beaker, a flask, a cylinder, a test tube, an enpindorf tube, a centrifugation tube, a culture dish, a multiwell plate and a filter device.

10 63. The method of claim 58, wherein the microdevice is placed or immobilized on a surface.

64. The method of claim 60, wherein the plurality of microdevices is placed or immobilized on a surface.

15 65. The method of claim 60, wherein the presence, amount or identity of said moieties are detected simultaneously.

20 66. The method of claim 58, wherein the binding partner specifically binds to the moiety.

25 67. An array for detecting moieties, which array comprises a plurality of microdevices placed or immobilized on a surface, each of said microdevices comprises a photorecognizable coding pattern on a substrate and a binding partner that is capable of binding to a moiety to be detected, wherein at least one of said microdevices does not comprise an anodized metal surface layer.

68. The array of claim 67, wherein the binding partners specifically bind to the moieties.

30 69. A method for synthesizing a library, which method comprises:

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a) providing a plurality of microdevices, each of said microdevices comprises a substrate and a photorecognizable coding pattern on said substrate, wherein said photorecognizable coding pattern corresponds to an entity to be synthesized on said microdevice, wherein at least one of said microdevices does not comprise an anodized metal surface layer; and

b) synthesizing said entities on said microdevices, wherein said microdevices are sorted after each synthesis cycle according to said photorecognizable coding patterns,

whereby a library is synthesized, wherein each of said microdevices contains an entity that corresponds to a photorecognizable coding pattern on said microdevice and the sum of said microdevices collectively contains a plurality of entities that is predetermined before the library synthesis.

70. The method of claim 69, wherein the substrate comprises a material that is selected from the group consisting of silicon, plastic, glass, ceramic, rubber, polymer and a combination thereof.

71. The method of claim 69, wherein the shape of the substrate is selected from the group consisting of sphere, square, rectangle, triangle, circular disc, cube-like shape, cube, rectangular parallelepiped (cuboid), cone, cylinder, prism, pyramid, right-angled circular cylinder and other regular or irregular shape.

72. The method of claim 69, wherein the thickness of the substrate is from about 1 micron to about 10 microns.

73. The method of claim 69, wherein the substrate comprises a silicon layer and a metal layer.

74. The method of claim 69, wherein the photorecognizable coding pattern is the material composition of the substrate itself, a hole in the substrate or a substance

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immobilized on the substrate, said substance having an optical refractive property that is different from the optical refractive property of the substrate.

5 75. The method of claim 74, wherein the versatility of the photorecognizable coding pattern is caused by the shape, number, position distribution, optical refractive property, material composition, or a combination thereof, of the substrate, the hole(s), or the substance(s) immobilized on the substrate.

10 76. The method of claim 69, wherein the photorecognizable coding pattern is fabricated or microfabricated on the substrate.

15 77. The method of claim 74, wherein the substance is deposited by evaporation or sputtering.

20 78. The method of claim 69, further comprising an element that facilitates and/or enables manipulation of the microdevice and/or the microdevice/synthesized entity complex.

25 79. The method of claim 78, wherein the element is selected from the group consisting of a magnetic material, a conductive or insulating material, a material having high or low acoustic impedance and a charged material.

30 80. The method of claim 78, wherein the element facilitates and/or enables manipulation of the microdevice and/or the microdevice/synthesized entity complex by a physical force selected from the group consisting of a dielectrophoresis, a traveling-wave dielectrophoresis, a magnetic, an acoustic, an electrostatic, a mechanical, an optical radiation and a thermal convection force.

81. The method of claim 69, wherein the microdevices further comprise a molecular tag.

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82. The method of claim 81, wherein the molecular tag is a DNA sequence or an antibody.

5 83. The method of claim 69, wherein each of the microdevices contains a single synthesized entity.

10 84. The method of claim 69, wherein the synthesized entities are selected from group consisting of peptides, proteins, oligonucleotides, nucleic acids, vitamins, oligosaccharides, carbohydrates, lipids, small molecules, or a complex or combination thereof.

15 85. The method of claim 69, wherein the synthesized library comprises a defined set of entities that are involved in a biological pathway, belongs to a group of entities with identical or similar biological function, expressed in a stage of cell cycle, expressed in a cell type, expressed in a tissue type, expressed in an organ type, expressed in a developmental stage, entities whose expression and/or activity are altered in a disease or disorder type or stage, or entities whose expression and/or activity are altered by drug or other treatments.

20 86. The method of claim 69, wherein the synthesized library comprises a defined set of nucleic acid fragments.

25 87. The method of claim 86, wherein each of the nucleic acid fragments in the synthesized library comprises at least 10, 15, 20, 25, 50, 75, 100, 200 or 500 nucleotides.

88. The method of claim 69, wherein the synthesized library comprises a defined set of protein or peptide fragments.

30 89. A library that is synthesized according to the method of claim 69.

90. A method for generating an antibody library, which method comprises:

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- a) contacting the library of claim 89 with a plurality of antibodies;
 - b) selecting and/or recovering the antibodies that specifically bind to the entities of the library of claim 89.

5 91. The method of claim 90, wherein the plurality of antibodies is a phage display library.

 92. The microdevice of claim 1, which does not comprise a porous surface.

10 93. The microdevice of claim 1, which comprises a metal layer and a non-metal surface layer.

 94. The microdevice of claim 1, which comprises a hole as the photorecognizable coding pattern and said hole does not penetrate through the entire
15 depth of the substrate.

 95. The microdevice of claim 28, wherein the element facilitates and/or enables manipulation of the microdevice and/or a moiety/microdevice complex by a physical force that is not a magnetic force.

20 96. A two-dimensional optical encoder, which encoder comprises:

- a) a substrate; and
- b) a microfabricated or micromachined two-dimensional optical code on said substrate.

25 97. The encoder of claim 96, wherein the substrate comprises a material selected from the group consisting of silicon, silicon dioxide, glass, plastic, polymer, magnetic material, carbon, metal, oxidized metal and a composite thereof.

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98. The encoder of claim 96, wherein the two-dimensional code is selected from the group consisting of a grating, an aperture-based code and a black-white line-segment code.

5 99. A carrier for chemical synthesis, which carrier comprises a surface suitable for chemical synthesis, said surface comprises a microfabricated or micromachined two-dimensional optical code, and said optical code identifies a chemical reaction to be conducted on said surface and/or product of said chemical reaction.

10 100. The carrier of claim 99, which carrier has a shape selected from the group consisting of a cube, a rectangular parallelepiped (cuboid), a cone, a cylinder, a prism, a pyramid and a right-angled circular cylinder.

15 101. The carrier of claim 99, which carrier comprises a spherical portion and a flat portion, wherein said flat portion comprises a microfabricated or micromachined two-dimensional optical code and said spherical portion is used for chemical synthesis.

20 102. The carrier of claim 99, wherein the non-coding region of the carrier further comprise a chemical layer linked to the carrier surface via a cleavable linker.

25 103. The carrier of claim 102, wherein the cleavable linker is selected from the group consisting of an optically cleavable, an enzymatically cleavable and a thermally cleavable linker, and said cleavable linker allows for subsequent chemical synthesis reactions.

30 104. A carrier for labeling a substance, which carrier comprises a surface for binding or linking a substance, and a microfabricated or micromachined two-dimensional optical code on said surface, said optical code is used for identifying said substance linked or coupled to said carrier.

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105. The carrier of claim 104, which carrier comprises a spherical portion and a flat portion, wherein said flat portion comprises a microfabricated or micromachined two-dimensional optical code and said spherical portion is used for linking or coupling the substance.

106. The carrier of claim 104, which carrier has a shape selected from the group consisting of a cube, a rectangular parallelepiped (cuboid), a cone, a cylinder, a prism, a pyramid and a right-angled circular cylinder.

107. A method for conducting chemical synthesis on the two-dimensional optical encoder of claim 96, which method comprises:

- a) mixing a plurality of the two-dimensional optical encoders of claim 96, each encoder having a unique optical code representing the corresponding synthesis reaction(s) to be conducted and/or product(s) to be synthesized on said encoder;
- b) chemically modifying the non-encoding regions of the surface of the encoders;
- c) continuously passing the optical encoders through a sorting device capable of identifying the optical code on said optical encoders, and transporting or sorting the optical encoders into corresponding reaction chambers based on their optical codes;
- d) performing synthesis procedures on said optical encoders in their corresponding reaction chambers; and
- e) after each step of the synthesis, mixing the optical encoders and sorting the encoders in a sorting device into new, corresponding reaction chambers again based on the optical codes on said encoders and the subsequent requisite synthesis steps for said encoders, performing a new step of the synthesis until all requisite synthesis steps are performed.

108. The method of claim 107, wherein the sorting device comprise a microchannel that allows the passage of one and only one optical encoder at a time, the encoder suspended in a liquid solution is manipulated or controlled to pass through the

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microchannel via an applied force, and the encoder is monitored or detected by a code-reader that is located in the vicinity of the microchannel.

5 109. The method of claim 107, wherein the applied force on the optical encoder, or substances linked thereto, is selected from the group consisting of a traveling-wave dielectrophoresis force, a traveling-wave magnetic field-force and a traveling-wave acoustic wave-induced force, whereby said applied force causes the encoders to pass through the microchannel and be sorted.

10 110. The method of claim 107, wherein the applied force on the optical encoder, or substances linked thereto, is selected from the group consisting of an electroosmotic pumping force, a mechanical pumping force and an electrohydrodynamic pumping force, said applied forces are applied to the solution liquid of the reaction system, and said solution liquid carries the optical encoder and the linked substances
15 through the microchannel.

20 111. The method of claim 107, wherein after the identification of the optical codes on the optical encoders via the sorting device, the encoders are transported, based on the optical code signals that are read-out from the encoder, to different reaction chambers that are linked to the microchannels.

25 112. A chip, which chip comprises a plurality of microfabricated two-dimensional optical encoders of claim 96, each encoder having biological and chemical substance(s) linked thereto, and said biological and chemical substance(s) are capable of being identified by the optical code on each optical encoder.

30 113. The chip of claim 112, wherein the biological substances are selected from the group consisting of DNA, RNA, peptide, protein, antibody, antigen, sugar, lipid, cytokine, hormone, cell, bacteria, virus and a composite thereof.

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